510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K210212

B Applicant

Psychemedics Corporation

C Proprietary and Established Names

Psychemedics Homogeneous Enzyme Immunoassay for Amphetamines in Hair

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LAF	Class II	21 CFR 862.3610 - Methamphetamine Test System	TX - Clinical Toxicology
DKZ	Class II	21 CFR 862.3100 - Amphetamine test system	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Amphetamine and Methamphetamine

C Type of Test:

Qualitative Homogeneous Enzyme Immunoassay (HEIA)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Psychemedics homogeneous enzyme immunoassay (HEIA) for amphetamines in hair is an enzyme immunoassay system for the preliminary qualitative detection of methamphetamine in human head and body hair using a methamphetamine calibrator at 3 ng methamphetamine/10 mg hair or 5 ng methamphetamine/10 mg hair for the purpose of identifying methamphetamine use, and for the preliminary qualitative detection of amphetamine in human head and body hair using an amphetamine calibrator at 3 ng amphetamine/10 mg hair for the purpose of identifying amphetamine use. This is an in vitro diagnostic device intended exclusively for Psychemedics use only and is not for sale to anyone.

The Psychemedics HEIA Amphetamines Assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical test result. Liquid Chromatography/Mass Spectrometry/Mass Spectrometry (LC/MS/MS) is the preferred confirmatory method.

C Special Conditions for Use Statement(s):

OTC - Over The Counter

D Special Instrument Requirements:

The Olympus AU 640 analyzer was used for validation of the candidate assay.

The confirmation assay uses an AB Sciex 3200 LC/MS/MS linked to two LC-20AD Prominence Liquid Chromatograph Pumps and a LEAP PAL HTC-xt autosampler.

IV Device/System Characteristics:

A Device Description:

The Psychemedics homogeneous enzyme immunoassay (HEIA) test for amphetamines in hair consists of two parts; a pre-analytical hair treatment procedure (to extract amphetamines or methamphetamines from the solid hair matrix to a measurable liquid matrix) and the screening assay, the Psychemedics Amphetamines HEIA.

The Psychemedics Amphetamines HEIA consists of reagents R1 (anti-methamphetamine monoclonal antibody with substrate) and R2 (methamphetamine labeled recombinant G6PDH) for the detection of methamphetamine, and reagents R1 (anti-amphetamine monoclonal antibody with substrate) and R2 (amphetamine labeled recombinant G6PDH) for the detection of amphetamine.

The confirmation assay consists of an AB Sciex 3200 LC/MS/MS linked to two LC-20AD Prominence Liquid Chromatograph Pumps and a LEAP PAL HTC-xt autosampler.

B Principle of Operation:

Hair sample extracts are combined with methamphetamine antibody and methamphetamine-labeled G6PDH and amphetamine antibody and amphetamine-labeled G6PDH using a chemistry autoanalyzer. The assay is based on competition between the drug-labeled G6PDH and free drug from the extracted hair sample for a fixed amount of specific antibody binding sites. In the absence of free drug from the samples, the specific antibody binds the drug-labeled G6PDH and causes a decrease in enzyme activity. This phenomenon creates a direct relationship between the drug concentration in hair and enzyme activity. The enzyme activity is determined spectrophotometrically at 340 nm.

For samples that are presumptive positive by the screening assay, a new aliquot of the hair sample is weighed, washed extensively to remove externally derived methamphetamine and amphetamine, extracted by a different procedure and confirmed by LC/MS/MS for the presence of methamphetamine and amphetamine.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Psychemedics Microplate EIA For Amphetamine in Hair, Psychemedics Microplate EIA for Methamphetamine in Hair

B Predicate 510(k) Number(s):
K130811, K111927

C Comparison with Predicate(s):

Device & Predicate Device(s):	K210212	K130811
Device Trade Name	Psychemedics homogeneous enzyme immunoassay for amphetamine in hair	Psychemedics Microplate EIA for Amphetamine in Hair
General Device Characteristic Similarities		
Intended Use/Indications For Use	Preliminary qualitative detection of amphetamine in human head and body hair using an amphetamine calibrator of 3 ng/10 mg hair for the purpose of identifying amphetamine use	Same
Measurand	Amphetamine	Same
Sample Matrix	Human Hair	Same

Device & Predicate Device(s):	K210212	K130811
Type of Test	Enzyme Immunoassay	Same
Confirmation Method	LC/MS/MS	Same
General Device Characteristic Differences		
Method of Measurement	Automated Clinical Chemistry Analyzer at 340 nm	Microplate Reader at 450 nm
Extraction Method	Acidic aqueous buffer	Patented Digestion Method

Device & Predicate Device(s):	K210212	K111927
Device Trade Name	Psychemedics homogeneous enzyme immunoassay for amphetamine in hair	Psychemedics Microplate EIA for Methamphetamine in hair
General Device Characteristic Similarities		
Intended Use/Indications For Use	Preliminary qualitative detection of methamphetamine in human head and body hair using a methamphetamine calibrator of 3 ng/10 mg hair or 5 ng/10 mg hair for the purpose of identifying methamphetamine use.	Same
Measurand	Methamphetamine	Same
Sample Matrix	Human Hair	Same
Type of Test	Enzyme Immunoassay	Same
Confirmation Method	LC/MS/MS	Same

Device & Predicate Device(s):	K210212	K111927
General Device Characteristic Differences		
Method of Measurement	Automated Clinical Chemistry Analyzer at 340 nm	Microplate Reader at 450 nm
Extraction Method	Acidic aqueous buffer	Patented Digestion Method

VI Standards/Guidance Documents Referenced:

None provided.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were performed by spiking negative hair with previously LC/MS/MS validated calibrator and control solutions to achieve concentrations of negative, the cutoff calibrator of 3 ng methamphetamine/10 mg hair, 5 ng methamphetamine/10 mg hair, or 3 ng amphetamine/10 mg hair, and +/- 75%, +/-50% and +/-25% of the cutoff calibrator.

Candidate Assay Methamphetamine Reagents Intra-Assay and Inter-Assay Precision Summary, 3 ng Methamphetamine/10 mg Hair Calibrator					
Summary Intra-Assay Precision			**Summary Inter-Assay Precision**		
Level	NEG	POS	Level	NEG	POS
-100%	8	0	-100%	80	0
-75%	8	0	-75%	80	0
-50%	8	0	-50%	80	0
-25%	8	0	-25%	80	0
+25%	0	8	+25%	0	80
+50	0	8	+50	0	80
+75%	0	8	+75%	0	80
+100%	0	8	+100%	0	80

Candidate Assay Methamphetamine Reagents Intra-Assay and Inter-Assay Precision Summary, 5 ng Methamphetamine/10 mg Hair Calibrator					
Summary Intra-Assay Precision			**Summary Inter-Assay Precision**		
Level	NEG	POS	Level	NEG	POS
-100%	8	0	-100%	80	0
-75%	8	0	-75%	80	0
-50%	8	0	-50%	80	0
-25%	8	0	-25%	80	0
+25%	0	8	+25%	0	80
+50	0	8	+50	0	80
+75%	0	8	+75%	0	80
+100%	0	8	+100%	0	80

Candidate Assay Amphetamine Reagents Intra-Assay and Inter-Assay Precision Summary					
Summary Intra-Assay Precision			**Summary Inter-Assay Precision**		
Level	NEG	POS	Level	NEG	POS
-100%	8	0	-100%	80	0
-75%	8	0	-75%	80	0
-50%	8	0	-50%	80	0
-25%	8	0	-25%	80	0
+25%	0	8	+25%	0	80
+50	0	8	+50	0	80
+75%	0	8	+75%	0	80
+100%	0	8	+100%	0	80

Precision Studies for LC-MS/MS

Intra-assay Precision Around the Cutoff: 3 ng of Methamphetamine and Amphetamine per 10 mg Hair

Intra-assay precision was determined around the cutoff of 3 ng methamphetamine and amphetamine per 10 mg hair at each of the following concentrations: 50%, 75%, 100%, 125% and 150%. The concentrations of amphetamines evaluated for intra-assay precision around the cutoff were: 1.5, 2.25, 3.0, 3.75 and 4.5 ng analyte per 10 mg hair. The concentrations of amphetamines evaluated for intra-assay precision from LLOQ to ULOQ were: 0.0, 0.25, 0.50, 1.0, 3.0, 5.0, 10.0, 25.0 and 50 ng analyte per 10 mg hair.

Intra-assay Precision Around the 3 ng Analyte per 10 mg Hair Cutoff					
	ng analyte/10 mg hair				
Methamphetamine	1.5	2.25	3.0	3.75	4.5
Average	1.424	2.148	2.73	3.406	4.14
S.D	0.044	0.013	0.071	0.115	0.135
%C.V.	3.085	0.607	2.590	3.364	3.272
Amphetamine	1.50	2.25	3.00	3.75	4.50
Average	1.534	2.234	3.036	3.732	4.492
S.D	0.057	0.077	0.092	0.066	0.207
%C.V.	3.705	3.447	3.015	1.781	4.599

Intra-assay precision over the range of the assay for methamphetamine and amphetamine is provided in the following table.

Intra-assay Precision Over the Range of the Assay								
	ng analyte/10 mg hair							
Meth	0.25	0.5	1.0	3.0	5.0	10.0	25.0	50.0
Average	0.264	0.537	1.0208	2.88	5.002	10.82	25.16	46.34
S.D	0.0080	0.0153	0.0283	0.0982	0.0642	0.4550	0.6465	0.9965
%C.V.	3.05	2.85	2.78	3.41	1.28	4.20	2.57	2.15
Amp	0.25	0.5	1.0	3.0	5.0	10.0	25.0	50.0
Average	0.261	0.529	0.980	2.81	4.822	10.92	25.98	48.14
S.D	0.0120	0.0167	0.0321	0.1166	0.2461	0.3194	0.2490	0.9762
%C.V.	4.61	3.15	3.28	4.15	5.10	2.92	0.96	2.03

Inter-assay Precision Around the Cutoff: 3 ng of Methamphetamine and Amphetamine per 10 mg Hair

Inter-assay precision around the cutoff was determined at 1.5, 3.0 and 4.5 ng analyte per 10 mg of hair. Inter-assay precision was performed over 5 separate days, testing each respective sample concentration in quintuplicate. Inter-assay Precision of the 3 ng analyte per 10 mg Hair cutoff for methamphetamine and amphetamine is provided in the following table.

Inter-assay Precision						
ng Analyte/10 mg hair						
	Methamphetamine			Amphetamine		
	1.5	**3.0**	**4.5**	**1.5**	**3.0**	**4.5**
Avg	1.49	2.95	4.35	1.47	2.98	4.36
S.D.	0.0759	0.1614	0.1825	0.0809	0.1061	0.2265
%CV	5.08	5.47	4.20	5.51	3.56	5.20

Intra-assay Precision Around the Cutoff: 5 ng of Methamphetamine per 10 mg Hair

The concentrations of 5 methamphetamine samples evaluated for intra-assay precision around the cutoff were: 2.5, 3.75, 5.0, 6.25 and 7.5 ng analyte per 10 mg hair. The concentrations of amphetamines evaluated for intra-assay precision from LLOQ to ULOQ were the same as those evaluated for the 3 ng of methamphetamine per 10 mg hair cutoff.

Intra-Assay Precision Around the 5 ng Cutoff					
ng analyte/10 mg hair					
	2.5	3.75	5.0	6.25	7.5
Avg.	2.52	3.77	5.05	6.09	7.15
S.D.	0.086	0.066	0.118	0.224	0.147
%CV	3.402	1.764	2.329	3.669	2.061

Inter-assay precision around the 5 ng/10 mg hair cutoff for methamphetamine is shown in the following table.

Inter-assay Precision around the 5 ng Cutoff			
Methamphetamine			
ng analyte/10 mg hair			
	2.5	**5.0**	**7.5**
Average	2.42	4.93	7.14
S.D.	0.105	0.155	0.270
%CV	4.32	3.15	3.78

2. Linearity:

The screening immunoassays are qualitative tests. An evaluation of linearity is not applicable.

LC-MS/MS Linearity:

The following concentrations were analyzed: 0.0, 0.25, 0.50, 1.0, 3.0, 5.0, 10.0, 25.0 and 50 ng methamphetamine and amphetamine per 10 mg of hair.

All results were within 20% of the target concentrations. Agreement of the 5 determinations at each concentration was ≤10% CV. The regression coefficient was > 0.995. The actual data points deviated <20% from the regression line.

The LC-MS/MS assay is used only to determine if the concentration of the target analyte is above or below the cutoff. There are no clinical claims for concentrations other than the cutoff.

3. Analytical Specificity/Interference:

Cross Reactivity:

Samples consisting of 8 mg hair were added to various compounds to determine cross reactivity. Structurally similar compounds were tested individually in the the candidate assay using the methamphetamine and amphetamine reagents to an expected cross reactivity of 1% (e.g., for the 5 ng methamphetamine/10 mg hair calibrator to 500 ng cross reactor/10 mg hair, for the 3 ng methamphetamine or amphetamine/10 mg hair calibrator to 300 ng cross reactor/10 mg hair). Structurally similar compounds that cross reacted at 1% were then tested at decreasing concentrations until the compound produced a positive result against the methamphetamine or amphetamine calibrator. Structurally dissimilar compounds (100 ng/10 mg hair) were tested individually as cross-reactants in the candidate assay using the methamphetamine and amphetamine reagents.

The cross-reactivity of the following metabolites and methamphetamines structural analogs was evaluated by determining the minimum concentration that would result approximately equivalent to the 3.0 ng methamphetamine/10 mg hair and 5.0 ng methamphetamine/10 mg cutoffs.

Cross Reactivities, Methamphetamine 3 ng/10 mg Calibrator, Structurally Related Compounds and Metabolites		
Compound	% Cross Reactivity	Concentration Equivalent to 3.0 ng Methamphetamine/10 mg Hair
MDMA	81	3.7
Para-Methoxy Methamphetamine	50	6.0
1R, 2S Ephedrine	20	15
MDEA	12	25
R-Methamphetamine	2	150
D-Amphetamine	<1	>300
L-Amphetamine	<1	>300
MDA	<1	>300
Para-methoxy Amphetamine	<1	>300

Cross Reactivities, Methamphetamine 5 ng/10 mg Calibrator, Structurally Related Compounds and Metabolites		
Compound	% Cross Reactivity	Concentration Equivalent to 5.0 ng Methamphetamine/10 mg Hair
MDMA	83	6
Para-Methoxy Methamphetamine	50	10

Cross Reactivities, Methamphetamine 5 ng/10 mg Calibrator, Structurally Related Compounds and Metabolites		
Compound	% Cross Reactivity	Concentration Equivalent to 5.0 ng Methamphetamine/10 mg Hair
1R, 2S Ephedrine	20	25
MDEA	10	50
R-(-)-Methamphetamine	2	175
D-Amphetamine	<1	>500
L-Amphetamine	<1	>500
MDA	<1	>500
Para-methoxy Amphetamine	<1	>500

The sponsor did not observe cross reactivity in the candidate assay using the methamphetamine reagents with the following compounds:

Anhydroecgonine Methyl Ester, Atropine, Bupropion, Cotinine, Cannabinol, Chlorpheniramine maleate, O-Desmethylvenlafaxine, Desipramine, Doxylamine succinate, 1S, 2R Ephedrine, Naproxen, Nicotine, Nortriptyline, H-Propoxyphene, R,R-Pseudoephedrine, Thioridazine, Cis-Tramadol, Venlafaxine, (±)-11-nor-9-Carboxy-Δ9-THC, Pentazocine, Amoxicillin, Propranolol, Promethazine, Phenmetrazine, Phendimetrazine, Benzocaine, Ecgonine, Dextromethorphan, Amitriptyline, R-(-)-Phenylephrine, Glutethimide, Meprobamate, Lidocaine, Carbamazepine, Diazepam, Nordiazepam, AM-2201, JWH-019, JWH-081, JWH-122, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline, CP47.497, CP47.497 C8 Homologue, HU-211, JWH-200, JWH-250, Ibuprofen, Naproxen, Ethosuximide, (±)-Epinephrine, Norepinephrine, Barbital, Metanephrine, Normetanephrine, Methocarbamol, Alprazolam, Cimoticline, Citalopram, Clopidogrel Bisulfate, Fluconazole, Hydrochlorothiazide, Lamotrigine, L-Thyroxine, Methyl Phenidate, Omeprazole, Amlodipine Besylate, Atorvastatin, Azithromycin, Bupivacaine, Cetirizine, Dimenhydrinate, Lisinopril, Methsuximide, Phensuximide, N-Normethyl Suximide, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Mephyton, Ethotoin, Mephobarbital, PEMA, 10, 11-Dihydrocarbamazepine, Medazepam, Chlorpramazine, Flurazepam, Lorazepam, Temazepam, Bromazepam, Primidone, 5,5-Diphenyl Hydantoin, Triamterene, Nordoxepin, Oxazepam, Levitriacetam, Metformin, Phenytoin, R-Phenylephrine, Sertraline, Topiramate, Zolpidem Tartrate, Vanilmandelic Acid, 5-Hydroxy Indole-3- Acetic Acid, Homovanilic Acid.

The cross reactivity of the following metabolites and amphetamines structural analogs was evaluated by determining the minimum concentration that would result approximately equivalent to the 3.0 ng amphetamine/10 mg hair cutoff.

Cross Reactivities of Structurally Related Compounds and Metabolites		
Compound	% Cross Reactivity	Concentration Equivalent to 3.0 ng Amphetamine/10 mg Hair
MDA	100	3.0
Phentermine	25	12
D-Methamphetamine	<1	>300
MDMA	<1	>300
Phenmetrazine	<1	>300
1R, 2S Ephedrine	<1	>300

The sponsor did not observe cross reactivity in the candidate assay using the amphetamine reagents with the following compounds:

Anhydroecgonine Methyl Ester, Atropine, Bupropion, Cotinine, Cannabinol, Chlorpheniramine maleate, O-Desmethylvenlafaxine, Desipramine, Doxylamine succinate, 1S, 2R Ephedrine, Naproxen, Nicotine, Nortriptyline, H-Propoxyphene, R,R-Pseudoephedrine, Thioridazine, Cis-Tramadol, Venlafaxine, (±)-11-nor-9-Carboxy-Δ9-THC, Pentazocine, Amoxicillin, Propranolol, Promethazine, Phenmetrazine, Phendimetrazine, Benzocaine, Ecgonine, Dextromethorphan, Amitriptyline, R-(-)-Phenylephrine, Glutethimide, Meprobamate, Lidocaine, Carbamazepine, Diazepam, Nordiazepam, AM-2201, JWH-019, JWH-081, JWH-122, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline, CP47.497, CP47.497 C8 Homologue, HU-211, JWH-200, JWH-250, Ibuprofen, Naproxen, Ethosuximide, (±)-Epinephrine, Norepinephrine, Barbital, Metanephrine, Normetanephrine, Methocarbamol, Alprazolam, Cimoticline, Citalopram, Clopidogrel Bisulfate, Fluconazole, Hydrochlorothiazide, Lamotrigine, L-Thyroxine, Methyl Phenidate, Omeprazole, Amlodipine Besylate, Atorvastatin, Azithromycin, Bupivacaine, Cetirizine, Dimenhydrinate, Lisinopril, Methsuximide, Phensuximide, N-Normethyl Suximide, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Mephyton, Ethotoin, Mephobarbital, PEMA, 10, 11-Dihydrocarbamazepine, Medazepam, Chlorpramazine, Flurazepam, Lorazepam, Temazepam, Bromazepam, Primidone, 5,5-Diphenyl Hydantoin, Triamterene, Nordoxepin, Oxazepam, Levitriacetam, Metformin, Phenytoin, R-Phenylephrine, Sertraline, Topiramate, Zolpidem Tartrate, Vanilmandelic Acid, 5-Hydroxy Indole-3- Acetic Acid, Homovanilic Acid.

Interference Studies

The following compounds (100 ng/10 mg hair) were tested at the methamphetamine cutoff at 3 ng and 5 ng/10 mg hair, the amphetamine cutoff of 3 ng analyte per 10 mg hair, and at +/- 50% of these cutoffs to determine which of them might interfere in the assay and to what degree and were found to have no interference with the candidate assay using the methamphetamine and amphetamine reagents.

Anhydroecgonine Methyl Ester, Atropine, Bupropion, Cotinine, Cannabinol, Chlorpheniramine maleate, O-Desmethylvenlafaxine, Desipiramine, Doxylamine Succinate, 1S, 2R-Ephedrine, Naproxen, Nicotine, Nortriptyline, Propoxyphene, R,R-Pseudoephedrine, Thioridazine, Cis-Tramadol, Venlafaxine HCl, 8-(-)-11-nor-9-caroxy-delta-9 THC, 11-nor-9-carboxy-delta-9 THC, Amoxicillin, Propanolol, Promethazine, Phenmetrazine, Phendimetrazine, Benzocaine, Ecgonine, Metanephrin, Glutethimide, Meprobamate, Methyprylon, Carbamazepine, Diazepam, Nordiazepam, Oxazepam, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline, Amitryptiline, Dextromethorphan, Lidocaine, Methocarbamol, Nordoxepin, Pentazocine, Phenylephrine, Triamterene, Ethosuximide, α-Methyl-α-propylsuccinimide, Metharbital, Barbital, Methsuximide, Phensuximide, N-Normethylsuximide, Mephenytoin, Ethytion, Mephobarbital, PEMA, Phenobarbital, Methyl PEMA, 10, 11-Dihydrocarbamazepine, Primidone, Carbamazepine, 5,5-Diphenylhydantoin, 4-Methylprimidone, Glutethimide, Methaqualone, Chlorpromazine, Flurazepam, AM-2201, JWH-019, JWH-081, JWH-122, CP47, 497 (±), CP 47, 497 (±) C8 Homologue, HU-211, JWH-200, JWH-250, Acetominophen, Caffeine, Chlorpheniramine, Ibuprofen, Naproxen, R,R-(-)-Pseudoephedrine, Epinephrine (±), Norepinephrine (±), normetanephrine (±), Alprazolam, Cimetidine, Citalopram HBr, Clonazepam, Clopidogrel Bisulfate, Fluconazole, Hydrochlorothiazide, Lamotrigine, L-Thyroxine, Methylphenidate HCl, Omeprazole, Amlopidine Besylate, Atorvastatin Calcium Salt, Azithromycin Dihydrate, Bupivacaine HCl, Cetirizine Di-HCl, Dimenhydrinate, Lisinopril Dihydrate, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Medazepam, Lorazepam, Temazepam, Bromazepam, Carbamazepine, Levetiracetam, Metformin HCl, Phenobarbital, Phenytoin, R-(-)-Phenylephrine HCl, Sertraline HCl, Topiramate, Zolpidem Tartrate, Zonisamide, 11-nor-9-caroxy-delta-8 THC, Streptomycin Solution, Procaine, Erythromycin, Penicillin G, Mepivacaine, Vanilmandelic Acid (±), 5-Hydroxyindole-3-Acetic Acid, Homovanilic Acid.

Immunoassay: Effect of cosmetic treatments

Head hair samples negative for methamphetamines and amphetamines and head hair samples positive for methamphetamines and amphetamines were treated with the following cosmetic treatments: permanent wave, relaxer, dye (which includes bleach), and shampoo. The study included 5 amphetamines-negative samples and 4 amphetamines-positive samples with each of the treatments along with 5 methamphetamines-negative and 4 methamphetamines-positive samples with the exception of permed methamphetamines negative samples which contained 4 negative samples. The results were compared to the same samples without treatments. All of the positive samples were previously analyzed by the confirmation procedure for amphetamines and methamphetamines. After the treatments these samples and an aliquot of the same hair samples untreated were extracted for amphetamines and methamphetamines analysis and then assayed by the candidate assay using the methamphetamine and amphetamine reagents. The results with and without treatment are compared to detect interference in the assay or loss of drug due to the treatments. No negative samples turned positive, and no positive samples became negative.

Specificity of the LC-MS/MS method

An interference study was conducted for the LC-MS/MS method by spiking potential interferents into negative hair specimens that did not contain any drug, and individually into hair specimens containing drug. Two aliquots of each compound or mix of compounds were analyzed with 2.0 ng methamphetamine and 1.2 ng amphetamine per 10 mg hair, and one without methamphetamine and amphetamine. The sponsor concluded that the potentially interfering compounds listed below did not cross-react or cause interference with the LC-MS/MS assay.

The following compound was tested at 2000 ng/10mg hair: Warfarin.

The following compounds were tested at 500 ng/10mg hair: Gabapentin, Pregabalin, Salicylic Acid, Valproic Acid, Vigabatrin, Acetaminophen, (-)-Cotinine, S-(-)-Nicotine, Caffeine.

The following compounds were tested at 200 ng/10mg hair: Morphine, Oxycodone, Codeine, Cocaine, Phencyclidine, S-(+)-Methamphetamine, S-(+) Amphetamine, (±)-Methadone, Phenobarbital, Phenytoin, R-(-)-Phenylephrine HCl, Carbamazepine, Salicylic Acid, Valproic Acid, Oxcarbazepine, Buprenorphine, Cis-Tramadol HCl, Hydrocodone, Hydromorphone, Meperidine, Naloxone, Naltrexone, Oxymorphone, Aripiprazole, Lacosamide, Oxocarbazepine, Rufinamide.

The following compounds were tested at 100 ng/ 10mg hair: Carbamazepine, Levetiracetam, Metformin HCl, Phenobarbital, Phenytoin, R-(-)-Phenylephrine HCl, Sertraline HCl, Topiramate, Zolpidem Tartrate, Zonisamide, Carbamazepine, Levetiracetam, (+)-Propoxyphene.

The following compounds were tested at 50ng/10mg hair: Atorvastatin·Ca Salt, Azithromycin·2 H_2O, Bupivacaine HCl·H_2O, Dimenhydrinate, Lisinopril·2H_2O, Loratadine, Montelukast·Na Salt, Pioglitazone·HCl, Procainamide·HCl, Simvastatin, Ibuprofen, Naproxen, (+)-Propoxyphene.

The following compounds were tested at 25ng/10mg hair: Cetirizine·2HCl, Prednisolone.

The following compounds were tested at 20ng/10 mg hair: Clonazepam, Estazolam, Flurazepam, Flunitrazepam, Midazolam, Nitrazepam, Prazepam, Triazolam, Zolpidem, Phentermine, R, R-(-)-Pseudoephedrine, Meprobamate, Ibuprofen, Naproxen, Fentanyl.

The following compounds were tested at 2.5ng/10mg hair: Amlopidine Besylate

4. Assay Reportable Range:

An assay reportable range is not applicable for the candidate assay using the methamphetamine and amphetamine reagents because they are qualitative only.

The claimed reportable range for the analytes methamphetamine and amphetamine measured by the LC-MS/MS method are as follows: 0.25 ng/10 mg hair to 50 ng/10mg of hair.

This reportable range is supported by the linearity, precision, and lower limit of quantitation (LLOQ) studies.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Traceability: The methamphetamine and amphetamine calibrators are traceable to certified reference materials from a commercial source.

Sample Shipping Stability During Storage: Nine (9) methamphetamine positive samples remained positive after approximately 8 months in storage and after shipping twice coast to coast. Nine (9) amphetamine positive samples remained positive after approximately 6 months in storage and after shipping twice coast to coast.

6. Detection Limit:

The candidate screening test yield qualitative results only; therefore, a detection limit evaluation is not applicable. See section VII.A.1. above for performance around the candidate device cutoff.

Detection Limit of the LC-MS/MS method
The sponsor performed a study to determine the Lower limit of Quantitation (LLOQ) of the confirmatory LC-MS/MS assay for amphetamine and methamphetamine.

The LLOQ is the lowest claimed concentration that can be quantitated within 20% of the expected value for methamphetamine and amphetamine. This was found to be 0.25 ng/10 mg hair for methamphetamine and amphetamine.

7. Assay Cut-Off:

Refer to Precision Studies above.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Methamphetamine, 3 ng methamphetamine/10 mg hair calibrator

Samples positive or negative for methamphetamine were tested with the candidate assay using the methamphetamine reagents.

The hair samples were then tested using Psychemedics' LC/MS/MS confirmatory assay, to compare the Psychemedics HEIA results with the LC/MS/MS results. The studies documented the source of hair (head or body) and other demographics to include gender and hair color. The comparison of the candidate device using the methamphetamine reagent at the 3 ng/10 mg hair calibrator with LC/MS/MS is shown in the following table.

HEIA Result	LC/MS/MS Result, ng Methamphetamine/10 mg hair (% of cutoff calibrator)			
	< 1.5 (< 50% below cutoff)	1.5 – 2.99 (≥ 50% below cutoff to cutoff)	3.0 – 4.5 (cutoff to ≥ 50% above cutoff)	> 4.5 (> 50% above cutoff)
Positive	0	0	6	50
Negative	53	5	0	0

Methamphetamine, 5 ng methamphetamine/10 mg hair calibrator

Samples positive or negative for methamphetamine were tested with the candidate assay using the methamphetamine reagents.

The hair samples were then tested using Psychemedics' LC/MS/MS confirmatory assay, to compare the Psychemedics HEIA results with the LC/MS/MS results. The studies documented the source of hair (head or body) and other demographics to include gender and hair color. The comparison of the candidate device using the methamphetamine reagent at the 5 ng/10 mg hair calibrator with LC/MS/MS is shown in the following table.

HEIA Result	LC/MS/MS Result, ng Methamphetamine/10 mg hair (% of cutoff calibrator)			
	< 2.5 (< 50% below cutoff)	2.5 – 4.99 (≥ 50% below cutoff to cutoff)	5.0 – 7.5 (cutoff to ≥ 50% above cutoff)	> 7.5 (> 50% above cutoff)
Positive	0	0	8	37
Negative	45	4	0	0

Amphetamine, 3 ng Amphetamine/10 mg hair calibrator

Samples positive or negative for amphetamine were tested with the candidate assay using the amphetamine reagents.

The hair samples were then tested using Psychemedics' LC/MS/MS confirmatory assay, to compare the Psychemedics HEIA results with the LC/MS/MS results. The studies documented the source of hair (head or body) and other demographics to include gender and hair color. The comparison of the candidate device using the amphetamine reagent with LC/MS/MS is shown in the following table.

HEIA Result	LC/MS/MS Result, ng Amphetamine/10 mg hair (% of cutoff calibrator)			
	< 1.5 (< 50% below cutoff)	1.5 – 2.99 (≥ 50% below cutoff to cutoff)	3.0 – 4.5 (cutoff to ≥ 50% above cutoff)	> 4.5 (> 50% above cutoff)
Positive	0	0	6	42
Negative	42	6	0	0

Recovery from LC-MS/MS Analysis
The sponsor conducted a study to evaluate recovery for methamphetamine and amphetamine at concentrations above and below the cutoff (ng/10 mg hair). Eight sample tubes were prepared and analyzed by LC/MS/MS. Recovery of methamphetamine and amphetamine was approximately 100%.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.